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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/557,907	04/21/2000	Holly Horton	1530.0060004/EKS/EJH	9397

26111 7590 05/24/2005

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 05/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/557,907	HORTON ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,3-7,16-18,30-35,38-41,43,46-50,66,69,71-74,77,78 and 83-86 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,3-7,16-18,30-35,38-41,43,46-50,66,69,71-74,77,78 and 83-86 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Upon reconsideration, the allowance of this application has been withdrawn to make the following rejections. Prosecution on the merits is hereby reopened. This action is non-final.

Claims 1, 3-7, 16-18, 30-35, 38-41, 43, 46-50, 66, 69, 71-74, 77, 78 and 83-86 are pending and under consideration in the instant office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 3-7, 30-35, 38 and 43 are rejected under 35 U.S.C. 102(a) as being anticipated by Lawson (J. Interferon and Cytokine Res., May 1997, Vol. 17, pg 255-261).

Lawson injected plasmid DNA encoding IFN-α operably linked to the human β actin promoter or the CMVIE promoter in saline into the skeletal tibialis anterior muscle of mice. The injection resulted in physiologically significant amounts of IFN-α in the systemic circulation (pg 256, Fig. 1B; pg 257, col. 1, "Injection of DNA constructs"; "Circulating IFN protein levels in serum"; see also the specification on pg 4, lines 24-26).

Without evidence to the contrary, the serum levels obtained by Lawson (22 and 36 IU/ml) are inherently "an amount effective to treat said cancer" as claimed (see pg 259, Table 4). The phrase "treating cancer or metastasis thereof in a mammal" in the preamble of the independent claims is an intended use and does not bear patentable weight in considering the art because it does not have to occur. The method steps in the body of claim 1 do not require the mammal has a tumor, injecting the DNA plasmid into a tumor or a step of treating cancer. The body of the claim merely requires injecting DNA plasmid into the muscle of a mammal and obtaining an amount of INF-α in the blood stream of a mammal capable of treating cancer. Therefore, Lawson taught the steps claimed and obtained serum levels of 22 and 36 IU/ml of INF-α, which is inherently effective to treat cancer.

The INF-α gene (pg 256, Fig. A) described by Lawson inherently had a polyA and transcription termination signal as claimed (3) because the plasmid expressed biologically active IFN-α (pg 256, col. 2, lines 4-5).

The phrase "of treating cancer or metastasis thereof in a mammal" in the preamble is an intended use and does not bear patentable weight in considering the art because the plasmid does not have to be administered to a mammal with cancer. The body of the claim does not require administering the plasmid to a mammal with cancer or metastasis. The injection may be performed in mammals without cancer as described by Lawson, which meets the limitation in the body of the claim. Dependent claims 4-6 and 30-34 further limit the phrase in the preamble and do not bear patentable weight for the same reasons.

Dependent claims 5, 6, 30-34 are included because the limitations are dependent upon the phrase "of treating cancer or metastasis thereof in a mammal" in the preamble of claim 1. The limitations relate, therefore, to an intended use and do not bear patentable weight in considering the art because the plasmid does not have to be administered to a mammal with cancers listed in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1, 3, 4, 7, 30, 31, 35, 38, 43 and 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lawson (J. Interferon and Cytokine Res., May 1997, Vol. 17, pg 255-261) in view of Zhang of record (PNAS, April 1996, Vol. 93, pg 4513-4518).

For this rejection, claim 1 is being interpreted as though the DNA plasmid was injected into a mammal with cancer or metastasis thereof.

Lawson injected plasmid DNA encoding IFN-α operably linked to the human β actin promoter or the CMVIE promoter in saline into the skeletal tibialis anterior muscle of mice. The injection resulted in physiologically significant amounts of IFN-α in the systemic circulation (pg 256, Fig. 1B; pg 257, col. 1, "Injection of DNA constructs"; "Circulating IFN protein levels in serum"; see also the specification on pg 4, lines 24-26).

Without evidence to the contrary, the serum levels obtained by Lawson (22 and 36 IU/ml) are inherently "an amount effective to treat said cancer" as claimed (see pg 259, Table 4).

The INF-α gene (pg 256, Fig. A) described by Lawson inherently had a polyA and transcription termination signal as claimed (3) because the plasmid expressed biologically active IFN-α (pg 256, col. 2, lines 4-5).

Lawson did not administer the plasmid to a mouse with breast or melanoma cancer.

However, Zhang established breast or melanoma tumors in the breast or thigh of mice then injected a vector encoding INF into the mice three times resulting in tumor regression.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding INF-α into the muscle of a mouse as taught by Lawson, wherein the mouse had an established breast or melanoma tumor as described by Zhang. One or ordinary skill in the art at the time the invention was made would have been motivated to use the technique described by Lawson in the mice with tumors described by Zhang because Lawson suggested using the technique in disease models (pg 256, col. 1, lines 12-14), specifically tumor models (pg 260, col. 2, last sentence).

It also would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a vector encoding INF into a mouse with a tumor three times as taught by Zhang, wherein the vector was a plasmid encoding INF-α and was injected intramuscularly as described by Zhang. One or ordinary skill in the art at the time the invention was made would have been motivated to replace the viral vector encoding IFN-consensus of Zhang with the plasmid encoding IFN-α described by Lawson to avoid the pathogenicity of adenoviruses (pg 4513, col. 1, last line, of Zhang) and because Lawson suggested using the plasmid in disease models (pg 256, col. 1, lines 12-14), specifically tumor models (pg 260, col. 2, last sentence).

One of ordinary skill in the art at the time of filing would have had a reasonable expectation of successfully treating tumors in the mice described by Zhang using the technique of Lawson because the serum levels of IFN-α described by Lawson (22 and 36 IU/ml) were capable of treating cancer (see pg 259, Table 4). The serum levels described by Lawson indicate systemic delivery of INF-α, which would ultimately allow contact of INF-α with the tumor through the vasculature.

Claims 46-49 are included because injecting the vector three times as taught by Zhang is equivalent to injecting the plasmid before, during or after gene therapy, i.e. the first injection is followed by gene therapy (the second and third injections), the second injection is preceded and followed by gene therapy (the first and third injection, etc.)

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

2. Claims 1, 3, 7, 35, 38 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ogura (Cancer research, 1990 Aug 15, Vol. 50 (16) pg 5102-6) in view of Lawson (J. Interferon and Cytokine Res., May 1997, Vol. 17, pg 255-261).

For this rejection, claim 1 is being interpreted as though the DNA plasmid was injected into a mammal with cancer or metastasis thereof.

Ogura established tumors in mice then injected a chamber apparatus subcutaneously, wherein the chamber apparatus comprised fibroblasts transfected with a plasmid encoding INF-α into the tumors resulting in tumor regression (pg 5103, last full ¶). The tumors were made using the chronic myelocytic leukemia cell line, KU812

(pg 5102, last 4 lines). Ogura did not inject the vector intramuscularly in the absence of the fibroblasts.

However, Lawson injected plasmid DNA encoding IFN-α operably linked to the human β actin promoter or the CMVIE promoter in saline into the skeletal tibialis anterior muscle of mice. The injection resulted in physiologically significant amounts of IFN-α in the systemic circulation (pg 256, Fig. 1B; pg 257, col. 1, "Injection of DNA constructs"; "Circulating IFN protein levels in serum"; see also the specification on pg 4, lines 24-26). The serum levels obtained by Lawson (22 and 36 IU/ml) are effective to treat cancer (pg 259, Table 4). The INF-α gene (pg 256, Fig. A) described by Lawson inherently had a polyA and transcription termination signal as claimed (3) because the plasmid expressed biologically active IFN-α (pg 256, col. 2, lines 4-5).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding INF-α into the mouse with a tumor as taught by Ogura, wherein the plasmid was in the absence of cells and injected intramuscularly as described by Lawson. One or ordinary skill in the art at the time the invention was made would have been motivated to replace the cells transfected with a plasmid encoding IFN-α described by Ogura with plasmids encoding IFN-α described by Lawson to avoid the steps of transfecting cells with the plasmid and culturing the cells in vitro.

It also would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding INF-α into a mouse intramuscularly as taught by Lawson, wherein the mice had established myelocytic leukemia tumors as

described by Ogura. One or ordinary skill in the art at the time the invention was made would have been motivated to perform the technique of Lawson in the mice described by Ogura because Lawson suggested using the plasmid in disease models (pg 256, col. 1, lines 12-14), specifically tumor models (pg 260, col. 2, last sentence).

One of ordinary skill in the art at the time of filing would have had a reasonable expectation of successfully treating tumors in the mice described by Ogura using the technique of Lawson because the serum levels of IFN-α described by Lawson (22 and 36 IU/ml) were capable of treating cancer (see pg 259, Table 4). The serum levels indicate systemic delivery of INF-α, which would ultimately allow contact of INF-α with the tumor through the vasculature.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

3. Claims 66, 69, 71-73 78 and 83-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aoki (Human gene therapy, 1997 Jun 10, Vol. 8 (9) pg 1105-13) in view of Lawson (J. Interferon and Cytokine Res., May 1997, Vol. 17, pg 255-261) and Welander (Investigational New drugs, 1987, Vol. 5, Suppl, S47-59, abstract only).

Aoki established pancreatic tumors in the peritoneal cavity of mice then injected a plasmid encoding HSV-TK operably linked to a promoter in a cationic liposome into the peritoneal cavity of the mice resulting in tumor regression. Aoki did not inject a vector encoding IFN-α.

However, Lawson injected plasmid DNA encoding IFN-α operably linked to the human β actin promoter or the CMVIE promoter into mice resulting in IFN-α expression (pg 256, Fig. 1B; pg 257, col. 1, "Injection of DNA constructs"; "Persistence of IFN expression in muscle," "Circulating IFN protein levels in serum"; see also the specification on pg 4, lines 24-26). The INF-α gene (pg 256, Fig. A) described by Lawson inherently had a polyA and transcription termination signal as claimed (3) because the plasmid expressed biologically active IFN-α (pg 256, col. 2, lines 4-5).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding a protein capable of treating cancer in a cationic liposome into the peritoneal cavity of a mouse with a peritoneal tumor as taught by Aoki, wherein the plasmid encoded IFN-α as described by Lawson. One or ordinary skill in the art at the time the invention was made would have been motivated to replace the plasmid encoding HSV-TK described by Aoki with the plasmid encoding IFN-α described by Lawson to avoid the use of the suicide gene HSV-TK and because intraperitoneal injection of INF-α was known to have anti-tumor effect (Welander abstract, last 5 lines).

It also would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding INF-α into a mouse as taught by Lawson, wherein the mice had established tumors as described by Aoki. One or ordinary skill in the art at the time the invention was made would have been motivated to use the plasmid of Lawson mice with established peritoneal tumors as described by Aoki because Lawson suggested using the plasmid in established disease models (pg

256, col. 1, lines 12-14), specifically tumor models (pg 260, col. 2, last sentence). One of ordinary skill would have been motivated to inject the plasmid encoding INF-α described by Lawson intraperitoneally as described by Aoki to maximize the level of INF-α and the tumor cell exposure to INF-α as described by Welander.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

4. Claims 1, 3-7, 30-35, 39-41, 43 and 46-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okamoto (Gene Therapy, 1997, Vol. 4, pg 969-976) in view of Lawson (J. Interferon and Cytokine Res., May 1997, Vol. 17, pg 255-261).

Okamoto injected a plasmid encoding a protein operably linked to a promoter in a cationic liposome into the quadricep of mice (Fig. 1). The mice were immunized three times (pg 971, Fig. 2 caption). Okamoto did not inject a vector encoding IFN-α.

However, Lawson injected plasmid DNA encoding IFN-α operably linked to the human β actin promoter or the CMVIE promoter intramuscularly into mice resulting in IFN-α expression (pg 256, Fig. 1B; pg 257, col. 1, "Injection of DNA constructs"; "Persistence of IFN expression in muscle;" see also the specification on pg 4, lines 24-26). The INF-α gene (pg 256, Fig. A) described by Lawson inherently had a polyA and transcription termination signal as claimed (3) because the plasmid expressed biologically active IFN-α (pg 256, col. 2, lines 4-5).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding a protein in a liposome intramuscularly

into a mouse as taught by Okamoto, wherein the plasmid encoded IFN-α as described by Lawson. One or ordinary skill in the art at the time the invention was made would have been motivated to replace the plasmid encoding MAGE-3 taught by Okamoto with the plasmid encoding IFN-α described by Lawson to determine the immune response to IFN-α in vivo. It also would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a plasmid encoding INF-α into a mouse intramuscularly as taught by Lawson using an HVJ-liposome as described by Okamoto. One or ordinary skill in the art at the time the invention was made would have been motivated to add the HVJ-liposome described by Okamoto to the plasmid of Lawson because Okamoto taught HVJ-liposomes caused expression of the protein but plasmid alone did not (see abstract). One of ordinary skill in the art at the time the invention was made would have been motivated to use the plasmid of Lawson in the method of Okamoto because Lawson suggested using the plasmid in established models (pg 256, col. 1, lines 12-14).

The phrase "of treating cancer or metastasis thereof in a mammal" in the preamble of claim 1 is an intended use and does not bear patentable weight in considering the art because the plasmid does not have to be administered to a mammal with cancer. The body of the claim does not require administering the plasmid to a mammal with cancer or metastasis. The injection may be performed in mammals without cancer as described by Okamoto and Lawson, which meets the limitation in the body of the claim.

Dependent claims 4-6 and 30-34 have been included because they further limit the phrase in the preamble and do not bear patentable weight.

Claims 46-49 are included because injecting the vector three times is equivalent to injecting the plasmid before, during or after gene therapy, i.e. the first injection is followed by gene therapy (the second and third injections), the second injection is preceded and followed by gene therapy (the first and third injection, etc.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Upon reconsideration, the double patenting rejection based on Application 09/839,574, now US Patent 6,875,748, has been revived because the claims taken with the disclosure of '748 teaches all the missing limitations claimed in the instant

application and because the limitations of the amount and the salt "M-X" used for DNA delivery in claim 1 of '748 did not have to be included in view of Example 17 in '748.

Claims 1, 3, 4, 16, 17, 30-32, 35, 38-41, 43 and 46-49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 30, 31, 34, 35 38-44, 47, 48, 49, 51 and 52 of U.S. Patent No. 6,875,748 in view of the disclosure of '748.

Claim 1 of '748 is directed toward:

> a method for expressing a polypeptide in a vertebrate, comprising administering into a tissue or cavity of said vertebrate a composition comprising: (a) about 1 ng to about 30 mg of a polynucleotide in aqueous solution, wherein the polynucleotide expresses a polypeptide upon delivery to vertebrate cells in vivo; (b) a salt M-X dissolved in said aqueous solution at a molar concentration ranging from about 50 mM to about 250 mM, and reaction, association, and dissociation products thereof, wherein M is a cation selected from the group consisting of sodium and potassium, wherein X is an anion selected from the group consisting of phosphate, acetate, bicarbonate, sulfate, and pyruvate; and (c) an auxiliary agent selected from the group consisting of a poloxamer and a reverse poloxamer; wherein said aqueous solution contains chloride ion at a molar concentration ranging from 0 mM to about 50 mM, and wherein said polypeptide is expressed in the vertebrate in an amount sufficient to be detectable.

The protein delivered can be a therapeutic protein such as INF-α (claim 35). The claims also recite using a cationic lipid (claim 40), injecting a human (claim 42), injecting into skeletal muscle (claim 48) or the peritoneal cavity (claim 44). While the claims of '574 require delivering a polynucleotide using a salt "M-X" and a poloxamer or reverse poloxamer, the composition injected in the method claims of '574 are a species within the genus of compositions injected in the method claims in the instant application.

The claims of '574 do not require obtaining protein expression "in the blood stream of said mammal in an amount effective to treat said cancer" as required in claim 1 of the instant application.

However, col. 57, line 25, through pg 58, line 15, of '574 describes injecting a plasmid encoding IFN-α into the rectus femoris of mice with melanoma tumors. The specification of '574 also described detecting protein expression in the serum to levels equivalent to those described by applicants in the instant application. Therefore, the disclosure of '574 described protein levels in the serum of mice capable of treating cancer as claimed.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to deliver DNA encoding IFN-α as claimed in '574 to treat melanoma tumors as described in the disclosure of '574. One of ordinary skill in the art at the time the invention was made would have been motivated to use the claims of '574 to treat mice with tumors because the disclosure of '574 to inhibit tumor growth. There is no apparent reason why applicants were prohibited from claiming a method of treating cancer as in the instant claims or why applicants were limited to administering a nucleotide sequence with the amounts, the salt M-X, and a poloxamer or reverse poloxamer. The disclosure taught delivering naked plasmid DNA encoding IFN-α intramuscularly in the absence of these elements to treat melanoma in Example 17 (col. 57-58).

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Horton (PNAS, Feb. 1999, Vol. 96, pg 1553-1558).

Manthorpe cited above under the obviousness type double patenting rejection (US Patent 6,875,748; Application No: 09/839,574, filed 4-23-01 and having priority to 11-28-00) was not available as prior art at the time the invention claimed in the instant application was made. The claimed invention in the instant application was at least taught in parent application 09/196,313, filed 11-20-98 to which applicants claim priority (see for example pg 59). Therefore, Manthorpe (effective filing date = 11-28-00) was not available as prior art at the time the invention claimed in the instant application was made (effective filing date is at least 11-20-98).

Wolff (US Patent 6,228,844) claims a method for stimulating vascular growth in the heart of a vertebrate, comprising injecting into the myocardium of the vertebrate a noninfectious, nonintegrating DNA construct comprising a promoter operably linked to a DNA sequence encoding vascular endothelial growth factor; wherein said DNA construct is injected in an amount sufficient that uptake of said DNA construct into cardiac cells of the vertebrate occurs, and sufficient expression of said vascular endothelial growth factor results, to stimulate vascular growth; and wherein said DNA construct is free from association with transfection-facilitating proteins, viral particles, liposomal formulations, charged lipids, and calcium phosphate precipitating agents.

'844 suggested delivering interferons using DNA and delivering DNA to treat cancer. '844 did not teach IFN-α or obtaining expression levels of a protein in the serum that were capable of treating cancer by administering the DNA intramuscularly or into the peritoneal cavity as currently claimed.

Wolff (US Patent 6,706,694; Application No: 09/588,655) claims a method for delivering a physiologically active polypeptide to a vertebrate heart, comprising: administering in vivo into heart muscle of a vertebrate a composition comprising a DNA operably encoding said physiologically active polypeptide through association with a promoter which directs synthesis of said polypeptide in vertebrate heart cells, and a pharmaceutically acceptable carrier; wherein said polynucleotide is free from association with liposomal formulations, charged lipids, transfection-facilitating precipitating agents, and transfection-facilitating viral particles; wherein a sufficient amount of said composition is administered to allow incorporation of said polynucleotide into heart cells of said vertebrate; and wherein said polypeptide is expressed in the heart of said vertebrate. '694 suggested delivering interferons using DNA and delivering DNA to treat cancer. '694 did not teach IFN-α or obtaining expression levels of a protein in the serum that were capable of treating cancer by administering the DNA intramuscularly or into the peritoneal cavity as currently claimed. It is not readily apparent that administering polynucleotides to the heart as in '694 can be used to treat cancer or metastasis as claimed in the instant application.

US Application number 10/028,782 has been considered for potential double patenting; however, '782 is limited to administering RNA which is patentably distinct from administering a DNA plasmid as claimed in the instant invention.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER